CLAIMS

1. An isolated polypeptide having the sequence of DSP-16 recited in SEQ ID NO:2, or a variant thereof that differs in one or more amino acid deletions, additions, insertions or substitutions at no more than 50% of the residues in SEQ ID NO:2, such that the polypeptide retains the ability to dephosphorylate an activated MAP-kinase.

2. An isolated polynucleotide that encodes at least ten consecutive amino acids of a polypeptide having a sequence corresponding to SEQ ID NO:2.

3. An isolated polynucleotide that encodes at least fifteen consecutive amino acids of a polypeptide having a sequence corresponding to SEQ ID NO:2.

4. An expression vector comprising a polynucleotide according to claim 2 or 3.

5. A host cell transformed or transfected with an expression vector according to claim 4.

6. An isolated polynucleotide that encodes a polypeptide according to claim 1.

7. A polynucleotide according to claim 6, comprising the sequence recited in SEQ ID NO:1.

8. An expression vector comprising a polynucleotide according to claim 6.

9. A host cell transformed or transfected with an expression vector according to claim 8.

10. An antisense polynucleotide comprising at least 15 consecutive nucleotides complementary to a polynucleotide according to claim 6.

11. An isolated polynucleotide that detectably hybridizes to the complement of the sequence recited in SEQ ID NO:1 under conditions that include a wash in 0.1X SSC and 0.1% SDS at 50 °C for 15 minutes.

12. An expression vector comprising a polynucleotide according to claim 10 or claim 11.

13. A host cell transformed or transfected with an expression vector according to claim 12.

14. A method of producing a DSP-16 polypeptide, comprising the steps of:

(a) culturing a host cell according to claim 9 under conditions that permit expression of the DSP-16 polypeptide; and

(b) isolating DSP-16 polypeptide from the host cell culture.

15. An isolated antibody, or antigen binding fragment thereof, that specifically binds to a DSP-16 polypeptide having the sequence of SEQ ID NO:2.

16. An antibody or fragment thereof according to claim 15, wherein the antibody is a monoclonal antibody.

17. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 15 in combination with a physiologically acceptable carrier.

18. A method for detecting DSP-16 expression in a sample, comprising:

(a) contacting a sample with an antibody or an antigen-binding fragment thereof according to claim 15, under conditions and for a time sufficient to allow formation of an antibody/DSP-16 complex; and

(b) detecting the level of antibody/DSP-16 complex, and therefrom detecting the presence of DSP-16 in a sample.

19. A method according to claim 18, wherein the antibody is linked to a support material.

20. A method according to claim 18, wherein the antibody is linked to a detectable marker.

21. A method according to claim 18, wherein the sample is a biological sample obtained from a patient.

22. A method for detecting DSP-16 expression in a sample, comprising:

(a) contacting a sample with an antisense polynucleotide according to claim 10 or claim 11; and

(b) detecting in the sample an amount of DSP-16 polynucleotide that hybridizes to the antisense polynucleotide, and therefrom detecting DSP-16 expression in the sample.

23. A method according to claim 22, wherein the amount of DSP-16 polynucleotide that hybridizes to the antisense polynucleotide is determined using polymerase chain reaction.

24. A method according to claim 22, wherein the amount of DSP-16 polynucleotide that hybridizes to the antisense polynucleotide is determined using a hybridization assay.

25. A method according to claim 22, wherein the sample comprises an RNA or cDNA preparation.

26. A method for screening for an agent that modulates DSP-16 activity, comprising the steps of:

(a) contacting a candidate agent with a polypeptide according to claim 1, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to dephosphorylate a DSP-16 substrate, relative to a predetermined ability of the polypeptide to dephosphorylate the DSP-16 substrate in the absence of candidate agent;

and therefrom identifying an agent that modulates DSP-16 activity.

27. A method according to claim 26, wherein the DSP-16 substrate is a MAP-kinase.

28. A method according to claim 26, wherein the candidate agent is a small molecule.

29. A method according to claim 26, wherein the small molecule is present within a combinatorial library.

30. A method for screening for an agent that modulates DSP-16 activity, comprising the steps of:

(a) contacting a candidate agent with a cell comprising a DSP-16 promoter operably linked to a polynucleotide encoding a detectable transcript or protein, under conditions and for a time sufficient to permit interaction between the promoter and candidate agent; and

(b) subsequently evaluating the expression of the polynucleotide, relative to a predetermined level of expression in the absence of candidate agent;

and therefrom identifying an agent that modulates DSP-16 activity.

31. A method according to claim 30, wherein the polynucleotide encodes a DSP-16 polypeptide.

32. A method according to claim 30, wherein the polynucleotide encodes a reporter protein.

33. A method for modulating a proliferative response in a cell, comprising contacting a cell with an agent that modulates DSP-16 activity.

34. A method for modulating differentiation of a cell, comprising contacting a cell with an agent that modulates DSP-16 activity.

35. A method for modulating survival of a cell, comprising contacting a cell with an agent that modulates DSP-16 activity.

36. A method according to any one of claims 33-35, wherein the agent modulates a pattern of gene expression.

37. A method according to any one of claims 33-35, wherein the cell displays contact inhibition of cell growth.

38. A method according to any one of claims 33-35, wherein the cell displays anchorage independent growth.

39. A method according to any one of claims 33-35, wherein the cell displays an altered intercellular adhesion property.

40. A method according to claim 35, wherein the agent modulates apoptosis.

41. A method according to claim 35, wherein the agent modulates the cell cycle.

42. A method according to claim 32, wherein the cell is present within a patient.

43. A method for treating a patient afflicted with a disorder associated with DSP-16 activity, comprising administering to a patient a therapeutically effective amount of an agent that modulates DSP-16 activity.

44. A method according to claim 43, wherein the disorder is selected from the group consisting of Duchenne muscular dystrophy, cancer, graft-versus-host disease, autoimmune diseases, allergies, metabolic diseases, abnormal cell growth, abnormal cell proliferation and cell cycle abnormalities.

45. A DSP-16 substrate trapping mutant polypeptide that differs from the sequence recited in SEQ ID NO:2 in one or more amino acid deletions, additions, insertions or substitutions at no more than 50% of the residues in SEQ ID NO:2, such that the polypeptide binds to a substrate with an affinity that is not substantially diminished relative to DSP-16, and such that the ability of the polypeptide to dephosphorylate a substrate is reduced relative to DSP-16.

46. A substrate trapping mutant polypeptide according to claim 45, wherein the polypeptide contains a substitution at position 213 or position 244 of SEQ ID NO:2.

47. A method for screening a molecule for the ability to interact with DSP-16, comprising the steps of:

(a) contacting a candidate molecule with a polypeptide according to claim 1 under conditions and for a time sufficient to permit the candidate molecule and polypeptide to interact; and

(b) detecting the presence or absence of binding of the candidate molecule to the polypeptide, and therefrom determining whether the candidate molecule interacts with DSP-16.

48. A method according to claim 47, wherein the step of detecting comprises an affinity purification step.

49. A method according to claim 47, wherein the step of detecting comprises a yeast two hybrid screen or a screen of a phage display library.

50. An isolated polypeptide comprising the sequence of DSP-16 alternate form recited in SEQ ID NO:21, or a variant thereof that differs in one or more amino acid deletions, additions, insertions or substitutions at no more than 50% of the residues in SEQ ID NO:21, such that the polypeptide retains the ability to dephosphorylate an activated MAP-kinase.

51. An isolated polynucleotide that encodes at least ten consecutive amino acids of a polypeptide having a sequence corresponding to SEQ ID NO:21.

52. An isolated polynucleotide that encodes at least fifteen consecutive amino acids of a polypeptide having a sequence corresponding to SEQ ID NO:21.

53. An expression vector comprising a polynucleotide according to claim 51 or 52.

54. A host cell transformed or transfected with an expression vector according to claim 53.

55. An isolated polynucleotide that encodes a polypeptide according to claim 50.

56. A polynucleotide according to claim 55, comprising the sequence recited in SEQ ID NO:20.

57. An expression vector comprising a polynucleotide according to claim 55.

58. A host cell transformed or transfected with an expression vector according to claim 57.

59. An antisense polynucleotide comprising at least 15 consecutive nucleotides complementary to a polynucleotide according to claim 55.

60. An isolated polynucleotide that detectably hybridizes to the complement of the sequence recited in SEQ ID NO:20 under conditions that include a wash in 0.1X SSC and 0.1% SDS at 60 °C for 15 minutes.

61. An expression vector comprising a polynucleotide according to claim 59 or claim 60.

62. A host cell transformed or transfected with an expression vector according to claim 61.

63. A method of producing a DSP-16 alternate form polypeptide, comprising the steps of:

(a) culturing a host cell according to claim 58 under conditions that permit expression of the DSP-16 alternate form polypeptide; and

(b) isolating DSP-16 alternate form polypeptide from the host cell culture.

64. An isolated antibody, or antigen binding fragment thereof, that specifically binds to a DSP-16 alternate form polypeptide having the sequence of SEQ ID NO:21.

65. An antibody or fragment thereof according to claim 64, wherein the antibody is a monoclonal antibody.

66. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 64 in combination with a physiologically acceptable carrier.

67. A method for detecting DSP-16 alternate form expression in a sample, comprising:

(a) contacting a sample with an antibody or an antigen-binding fragment thereof according to claim 64, under conditions and for a time sufficient to allow formation of an antibody/DSP-16 alternate form complex; and

(b) detecting the level of antibody/DSP-16 alternate form complex, and therefrom detecting the presence of DSP-16 alternate form in a sample.

68. A method according to claim 67, wherein the antibody is linked to a support material.

69. A method according to claim 67, wherein the antibody is linked to a detectable marker.

70. A method according to claim 67, wherein the sample is a biological sample obtained from a patient.

71. A method for detecting DSP-16 alternate form expression in a sample, comprising:

(a) contacting a sample with an antisense polynucleotide according to claim 59 or claim 60; and

(b) detecting in the sample an amount of DSP-16 alternate form polynucleotide that hybridizes to the antisense polynucleotide, and therefrom detecting DSP-16 alternate form expression in the sample.

72. A method according to claim 71, wherein the amount of DSP-16 alternate form polynucleotide that hybridizes to the antisense polynucleotide is determined using polymerase chain reaction.

73. A method according to claim 71, wherein the amount of DSP-16 alternate form polynucleotide that hybridizes to the antisense polynucleotide is determined using a hybridization assay.

74. A method according to claim 71, wherein the sample comprises an RNA or cDNA preparation.

75. A method for screening for an agent that modulates DSP-16 alternate form activity, comprising the steps of:

(a) contacting a candidate agent with a polypeptide according to claim 50, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to dephosphorylate a DSP-16 alternate form substrate, relative to a predetermined ability of the polypeptide to dephosphorylate the DSP-16 alternate form substrate in the absence of candidate agent;

and therefrom identifying an agent that modulates DSP-16 alternate form activity.

76. A method according to claim 75, wherein the DSP-16 alternate form substrate is a MAP-kinase.

77. A method according to claim 75, wherein the candidate agent is a small molecule.

78. A method according to claim 75, wherein the small molecule is present within a combinatorial library.

79. A method for screening for an agent that modulates DSP-16 alternate form activity, comprising the steps of:

(a) contacting a candidate agent with a cell comprising a DSP-16 alternate form promoter operably linked to a polynucleotide encoding a detectable transcript or protein, under conditions and for a time sufficient to permit interaction between the promoter and candidate agent; and

(b) subsequently evaluating the expression of the polynucleotide, relative to a predetermined level of expression in the absence of candidate agent;

and therefrom identifying an agent that modulates DSP-16 alternate form activity.

80. A method according to claim 79, wherein the polynucleotide encodes a DSP-16 alternate form polypeptide.

81. A method according to claim 79, wherein the polynucleotide encodes a reporter protein.

82. A method for modulating a proliferative response in a cell, comprising contacting a cell with an agent that modulates DSP-16 alternate form activity.

83. A method for modulating differentiation of a cell, comprising contacting a cell with an agent that modulates DSP-16 alternate form activity.

84. A method for modulating survival of a cell, comprising contacting a cell with an agent that modulates DSP-16 alternate form activity.

85. A method according to any one of claims 82-84, wherein the agent modulates a pattern of gene expression.

86. A method according to any one of claims 82-84, wherein the cell displays contact inhibition of cell growth.

87. A method according to any one of claims 82-84, wherein the cell displays anchorage independent growth.

88. A method according to any one of claims 82-84, wherein the cell displays an altered intercellular adhesion property.

89. A method according to claim 84, wherein the agent modulates apoptosis.

90. A method according to claim 84, wherein the agent modulates the cell cycle.

91. A method according to claim 81, wherein the cell is present within a patient.

92. A method for treating a patient afflicted with a disorder associated with DSP-16 alternate form activity, comprising administering to a patient a therapeutically effective amount of an agent that modulates DSP-16 alternate form activity.

93. A method according to claim 92, wherein the disorder is selected from the group consisting of cancer, graft-versus-host disease, autoimmune diseases, allergies, metabolic diseases, abnormal cell growth, abnormal cell proliferation and cell cycle abnormalities.

94. A DSP-16 alternate form substrate trapping mutant polypeptide that differs from the sequence recited in SEQ ID NO:21 in one or more amino acid deletions, additions, insertions or substitutions at no more than 50% of the residues in SEQ ID NO:21, such that the polypeptide binds to a substrate with an affinity that is not substantially diminished relative to DSP-16 alternate form, and such that the ability of the polypeptide to dephosphorylate a substrate is reduced relative to DSP-16 alternate form.

95. A substrate trapping mutant polypeptide according to claim 94, wherein the polypeptide contains a substitution at position 213 or position 244 of SEQ ID NO:21.

96. A method for screening a molecule for the ability to interact with DSP-16 alternate form, comprising the steps of:

(a) contacting a candidate molecule with a polypeptide according to claim 50 under conditions and for a time sufficient to permit the candidate molecule and polypeptide to interact; and

(b) detecting the presence or absence of binding of the candidate molecule to the polypeptide, and therefrom determining whether the candidate molecule interacts with DSP-16 alternate form.

97. A method according to claim 96, wherein the step of detecting comprises an affinity purification step.

98. A method according to claim 96, wherein the step of detecting comprises a yeast two hybrid screen or a screen of a phage display library.